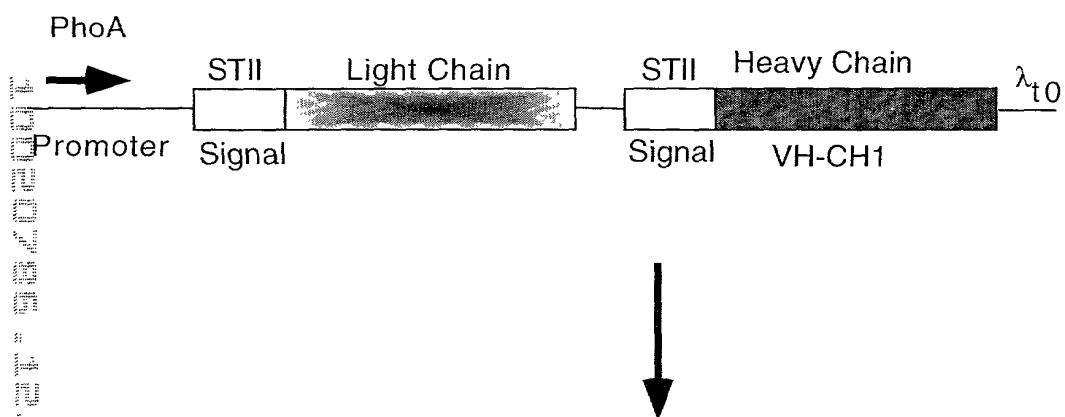


Fab Expression Vector pAK19



Full Length Antibody Expression Vector Derived from pAK19

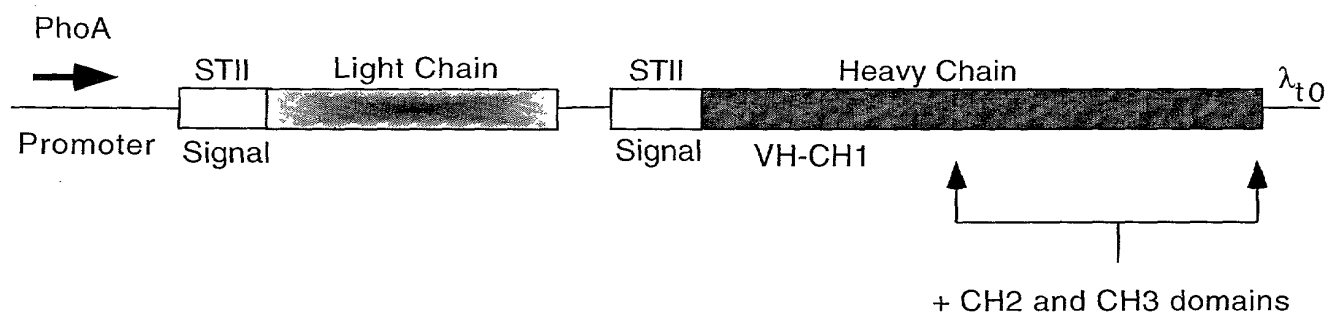


Figure 1

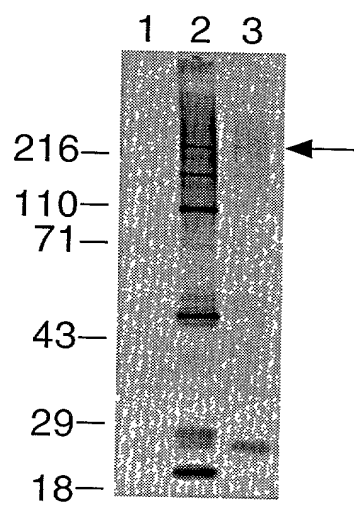


Figure 2

Polycistronic Constructs

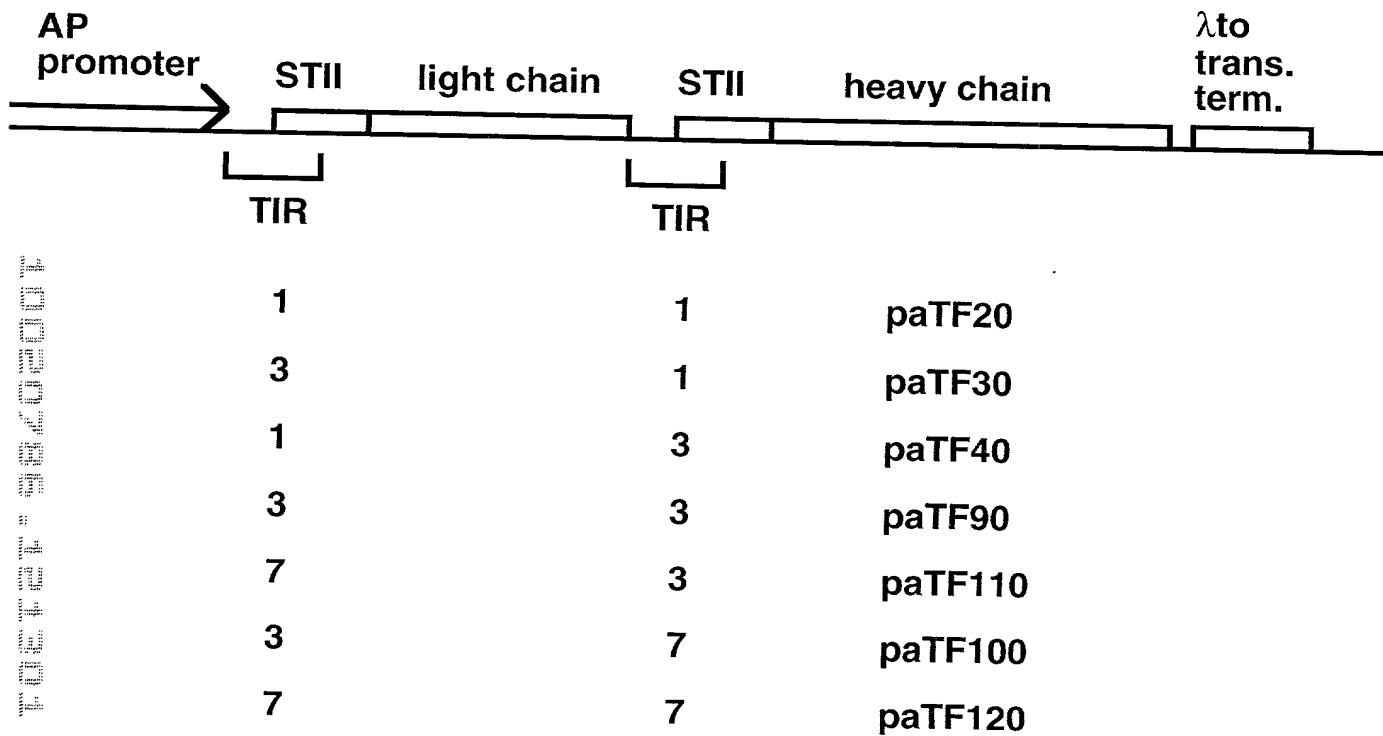


Figure 3.

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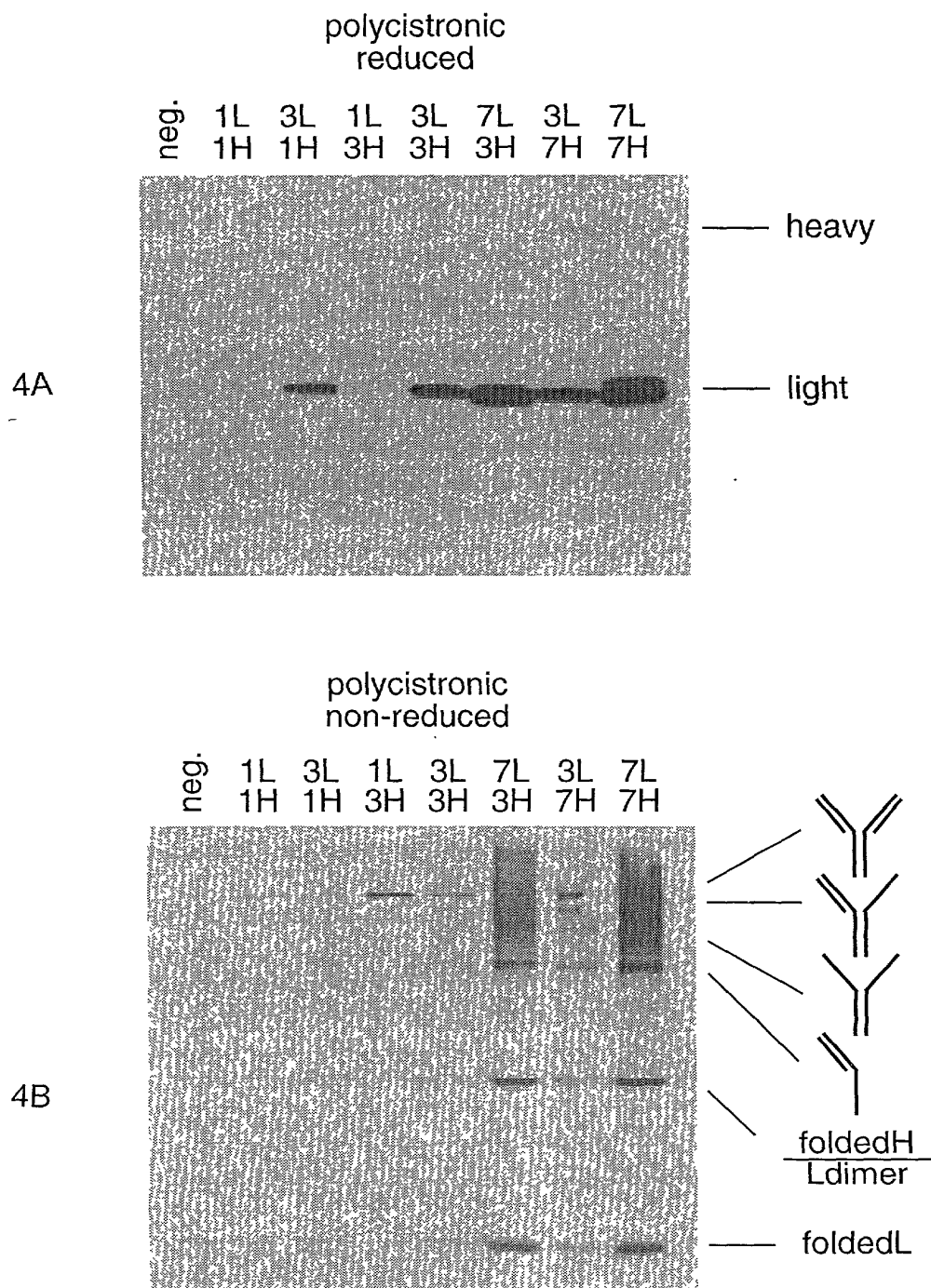
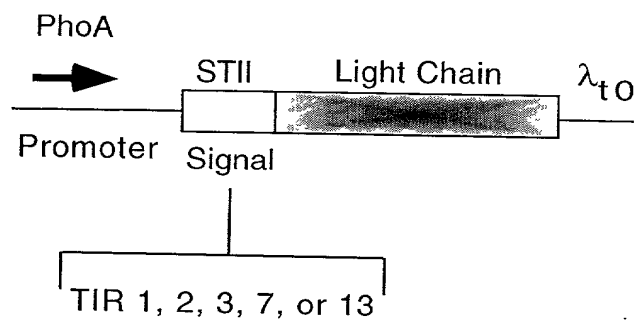


Figure 4

Light Chain Constructions



Heavy Chain Constructions

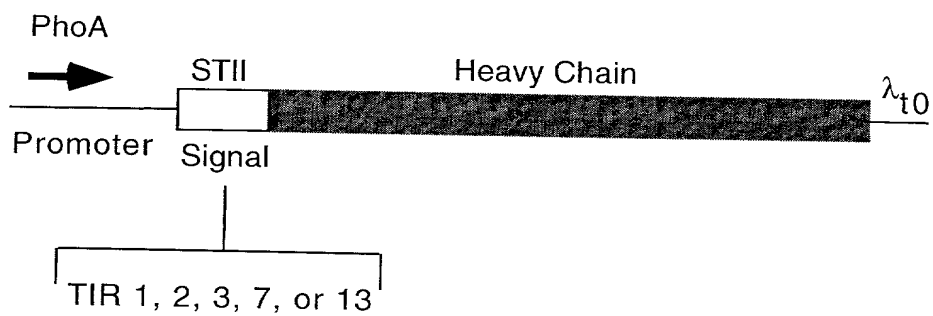


Figure 5

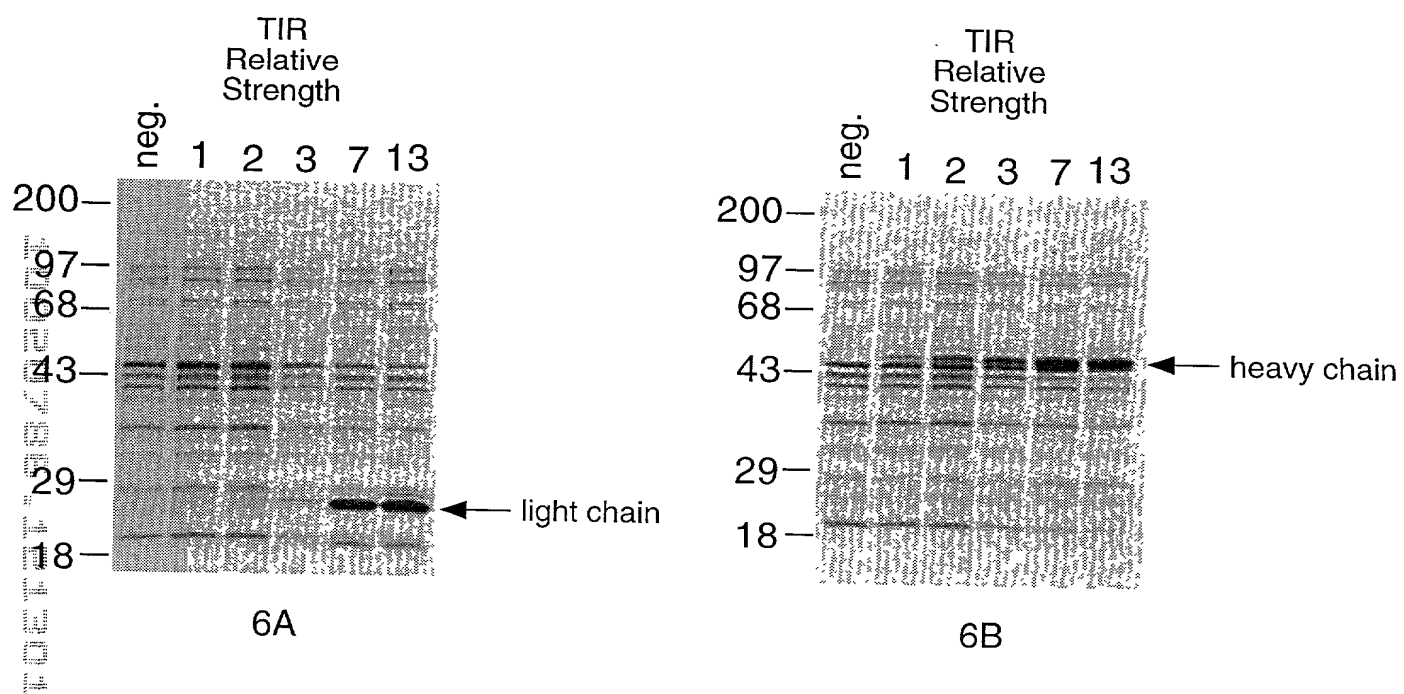


Figure 6

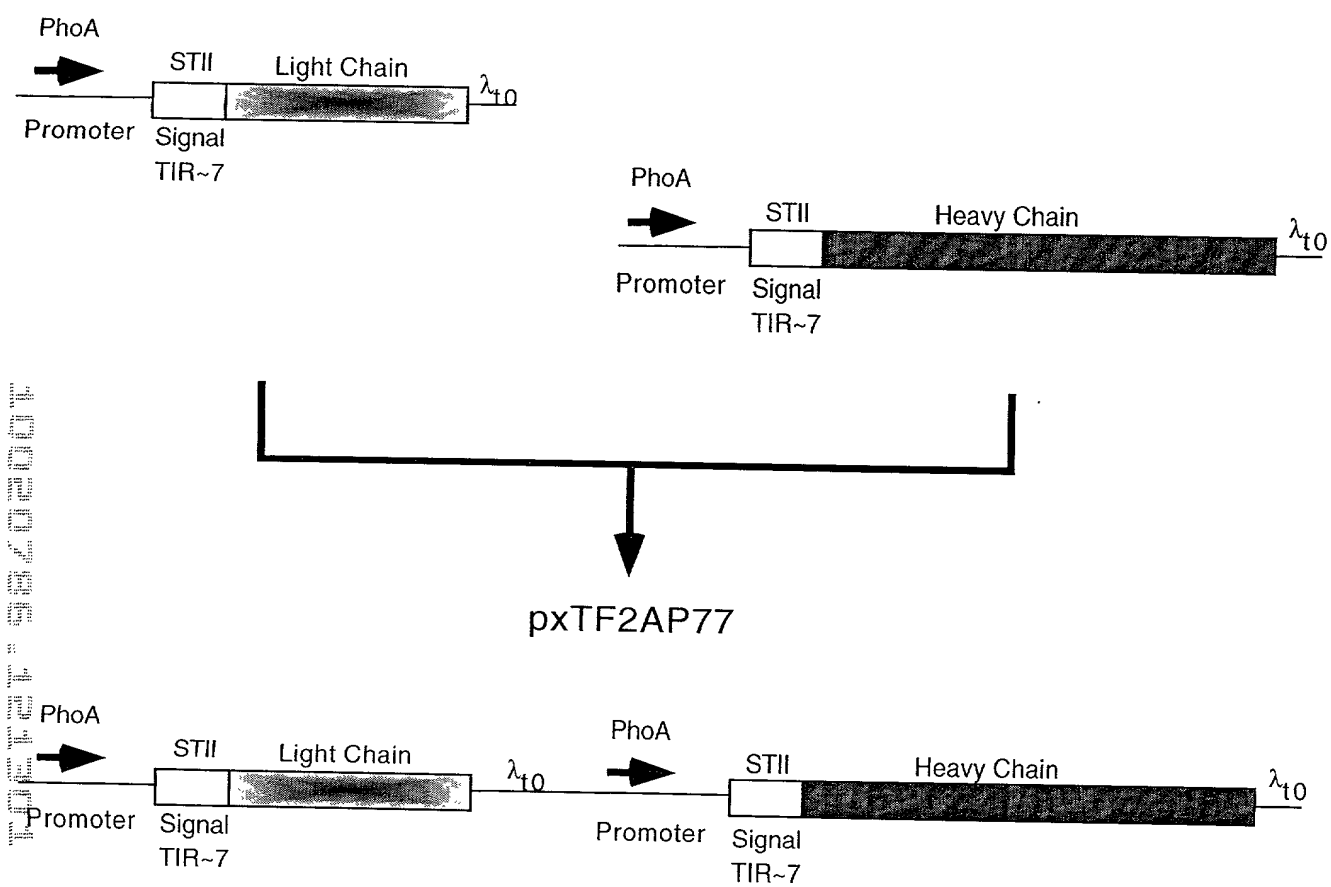


Figure 7

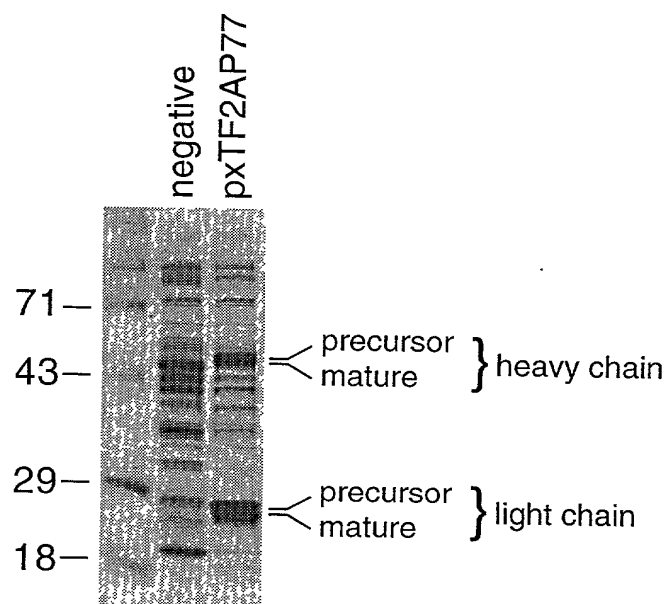


Figure 8

Separate Cistron Constructs

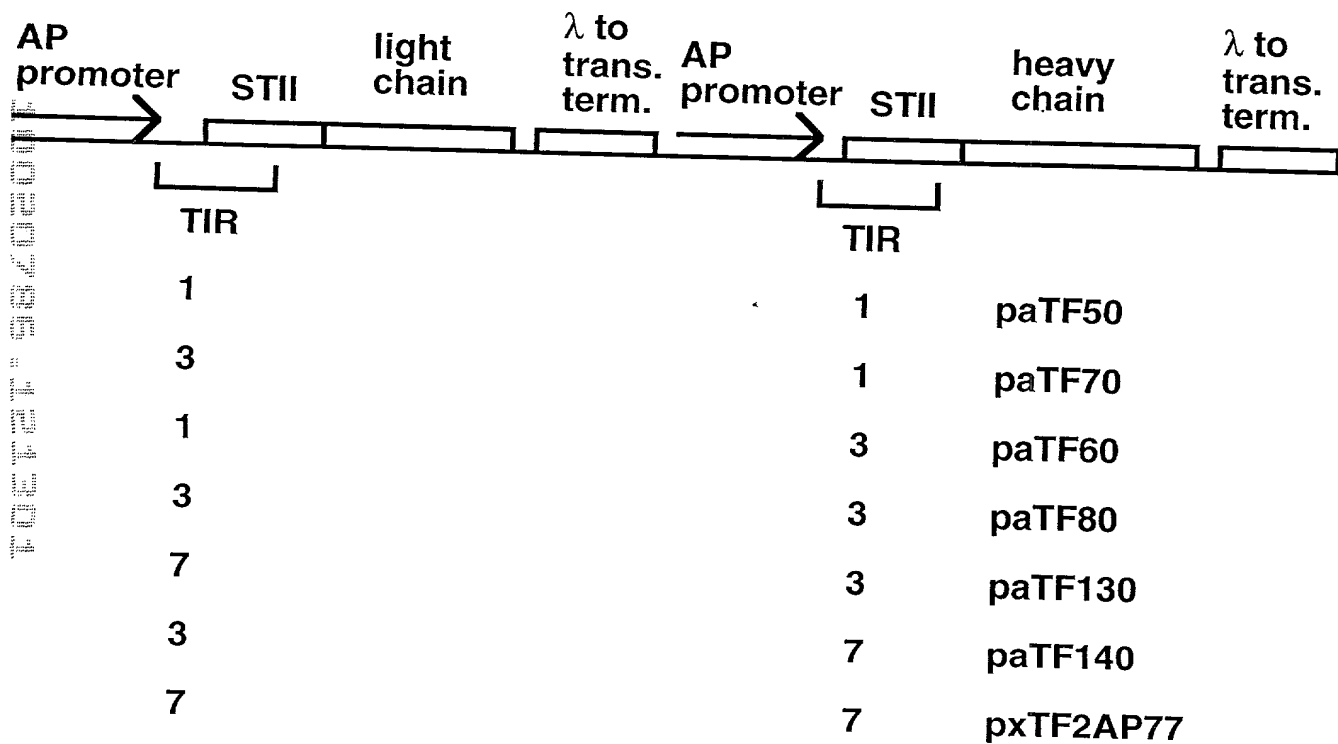


Figure 9

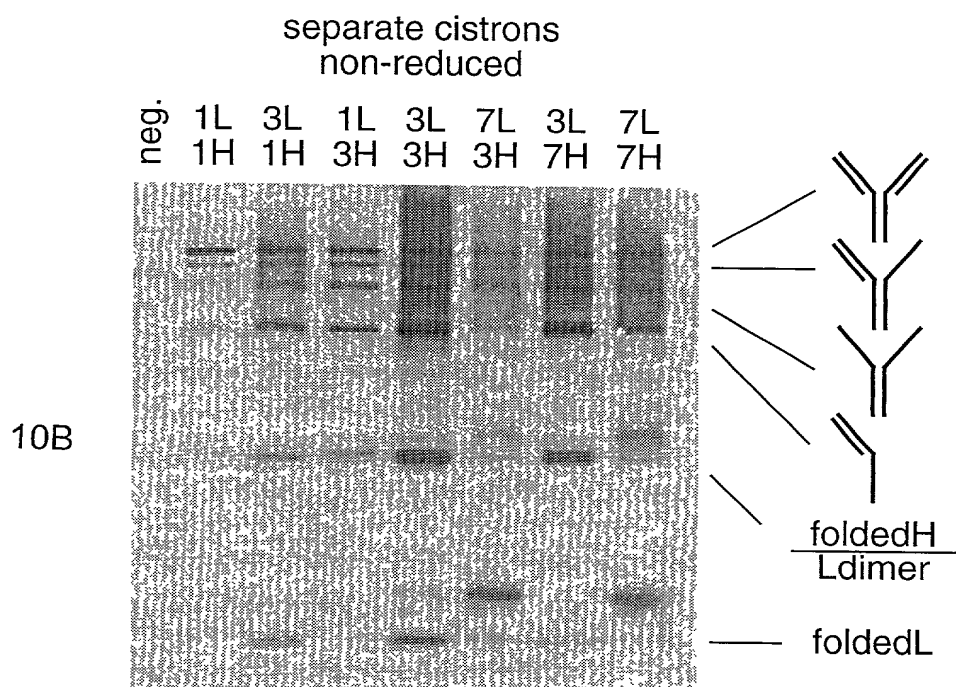
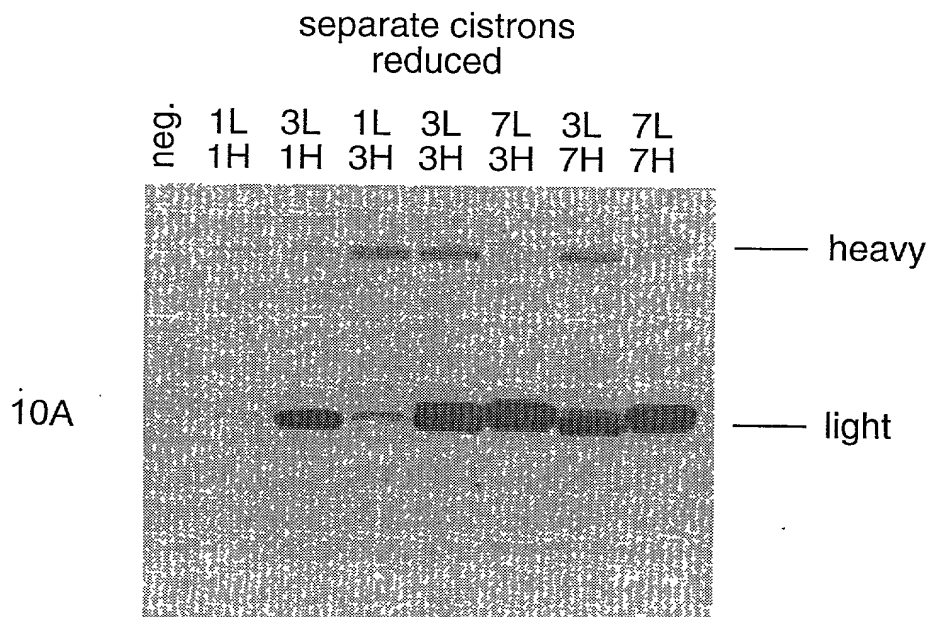
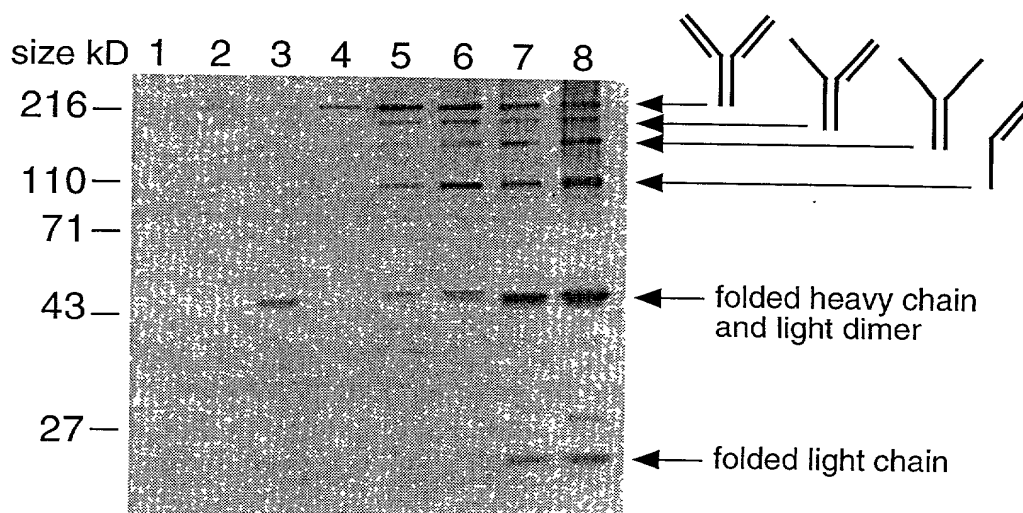


Figure 10



- 1) negative control
- 2) TIR 1-light, TIR 1-heavy, polycistronic
- 3) TIR 3-light, TIR 1-heavy, polycistronic
- 4) TIR 1-light, TIR 3-heavy, polycistronic
- 5) TIR 1-light, TIR 1-heavy, separate cistrons
- 6) TIR 1-light, TIR 3-heavy, separate cistrons
- 7) TIR 3-light, TIR 1-heavy, separate cistrons
- 8) TIR 3-light, TIR 3-heavy, separate cistrons

Figure 11

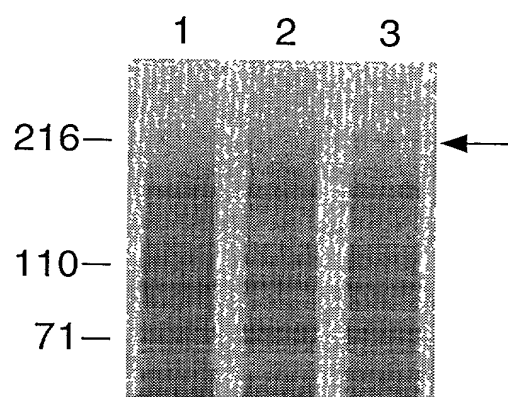


Figure 12

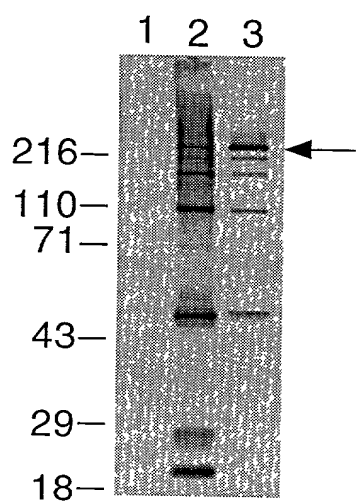


Figure 13

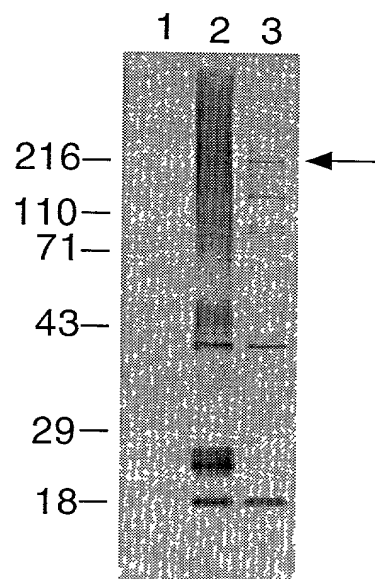


Figure 14

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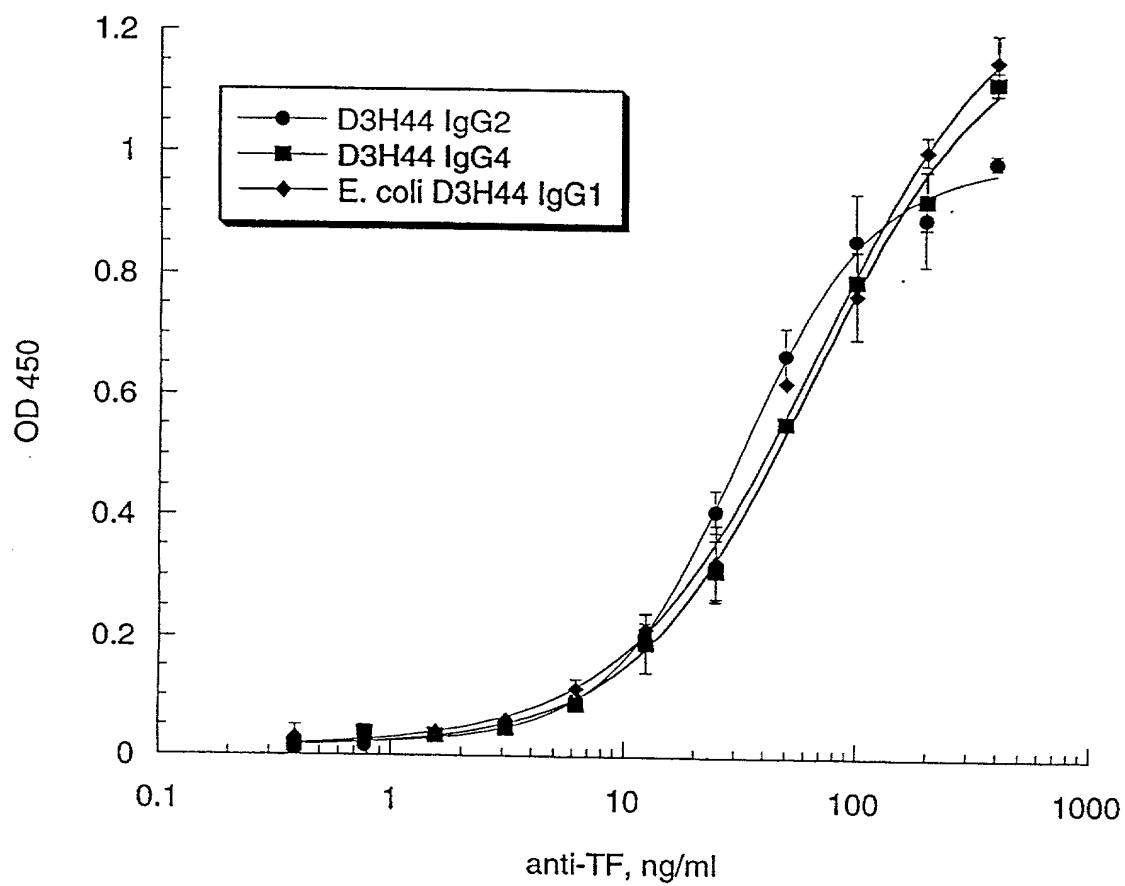


Figure 15

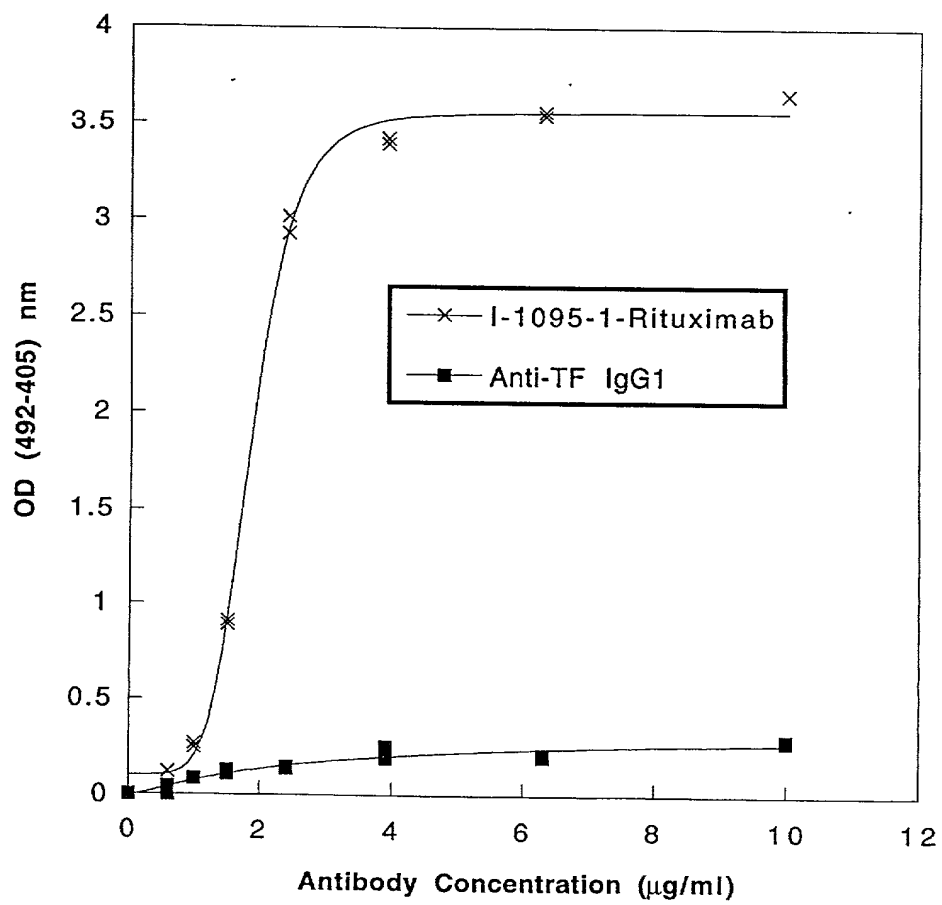


Figure 16

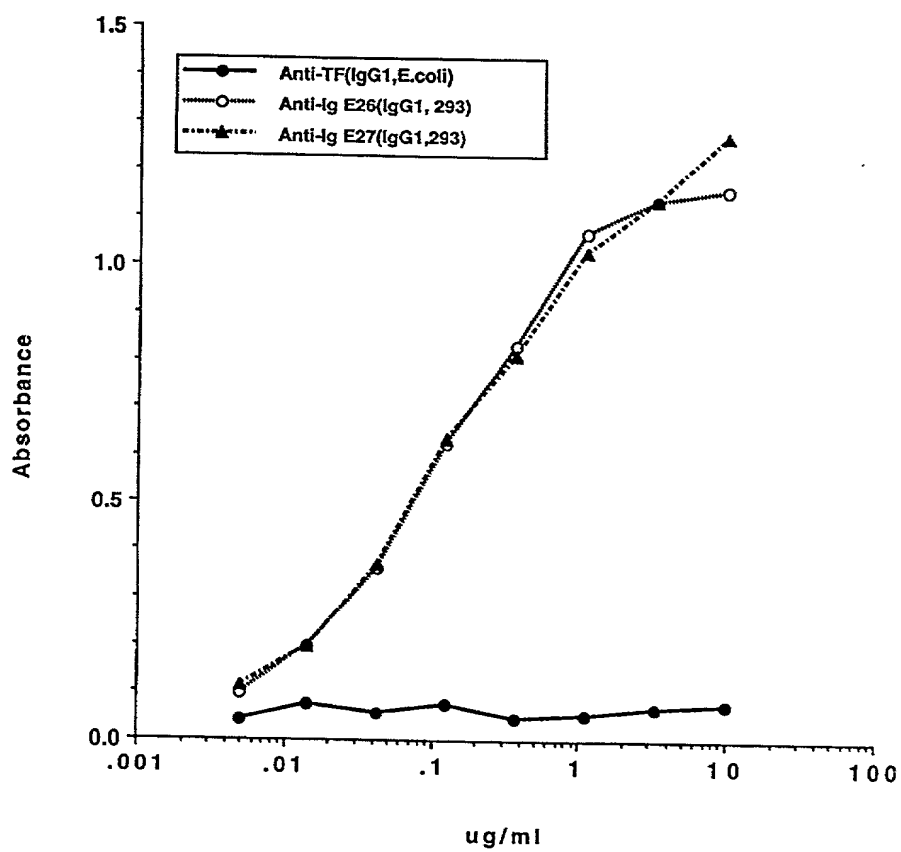


Figure 17

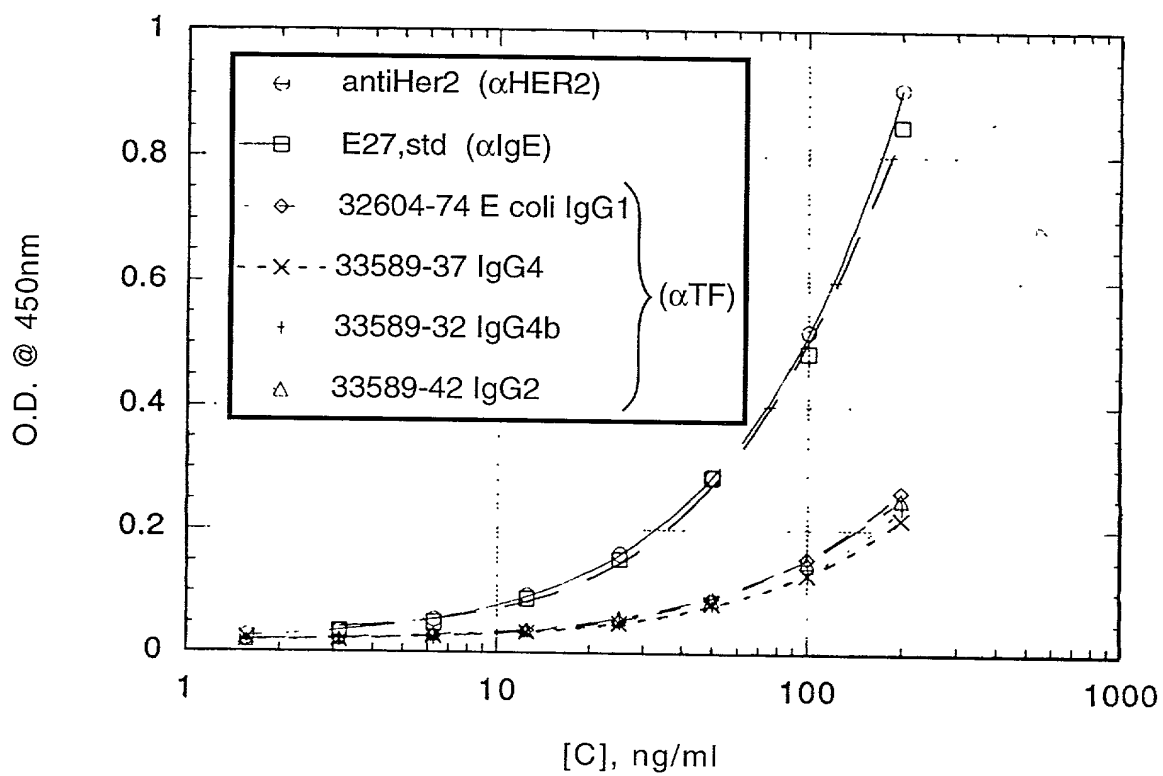


Figure 18

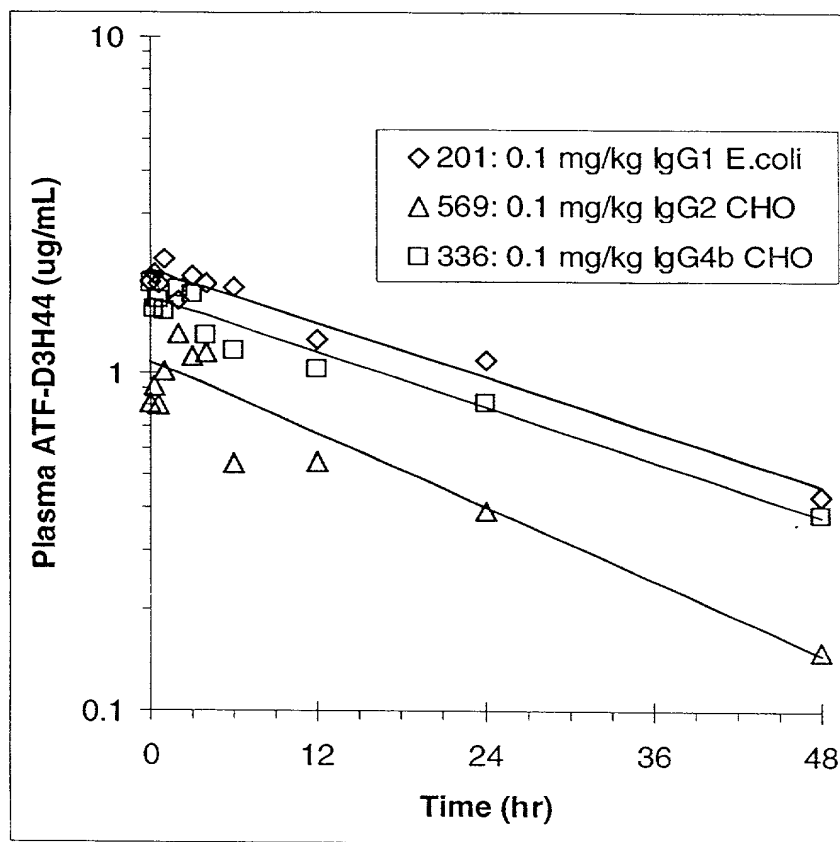


Figure 19

1 GAATTCACCT TCTCATACT TTGATAAGG AATACAGAC ATGAAAATC TCATTGCTCA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATGCC TTATGTCTG TACTTTTAG AGTAACGACT CAACAATAAA TTGGAACGGG TTTTCTTCTT TCTCAGCTTA

101 GAACCTGTG CGAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC CGGTCCATCT TCGAAACCTC TAATAGCAGT GAGCTTAGA AGCGTTTATC CGCGTTTATC TGGTTGTCG CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCGATGCCA GCATTCCCTGA CGAGATACG GAGCTGCTGC GCGATTACGT ARAAGAAGTTA TTGAAAGCATC CTCCTCAGTA
CCGCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGTATGCG CTCGACGACG CGTAATGCA TTTCTTCAAT AACCTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCAACA GCTGTCAATA AGTTGTACG CCGAGACCT ATAGTCGGCTT TGTCTTATTT TTTTATATGA TTTGTAACTA GTACGCAAGT
TTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATCGTTCA

401 TCACGTAAAA AGGTATCTTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT TTGATTCGTA CAAACGCGTA CGCTGATATC
AGTGCAATTT TCCCATAGAT CTTAATACCT CTTCCTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATACAGAT GTTTGCGCAT GCGACTATAG

1 M K N I A F L L A S M F V F S I A T N A Y A D I
^SIII Signal Sequence TIR-1 Anti-Tissue Factor Light Chain^

501 CAGATGACCC AGTCCCGAG CTCCTGTCC GCCTGTGTG GCGATAGGCT CACCATACC TGACAGGCCA GTGCGGACAT CAAGAGCTAT CTGAACCTGGT
GTCTACTGG TCAGGGGCTC GAGGACAGG CCGAGACACC CGCTATCCCA GTGCTAGTGG AGTCTCGGT CAGCGCTGTA GTTCTCGATA GACTTGACCA

26 Q M T Q S P S S L S A S V G D R V T I T C R A S R D I K S Y L N W Y

601 ATCAACAGAA ACCAGNAAA GCTCCGAAG TACTGATTTA CTATGCTACT AGTCTGCTG AAGGATGCC TTCTGCTTC TCTGATCCG GTTCTGGGAC
TAGTTGCTT TGGTCCCTTT CGAGGCTTC ATGACTAAAT GATACGATGA TCAGAGCGAC TTCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCCTG

60 Q Q K P G K A P K V L I Y A T S L A E G V P S R F S G S G T

701 SGATTACACT CTGACCATCA GCAGTCTGCA GCCAGAGAC TTCCGAACTT ATTACTGCT TCAGCAGCGA GAGTCTCCAT GGACATTTGG ACAGGTTACC
CCTAATGTGA GACTGTAGT CGTCTCTCTG AAGCGTTGAA TAATGACAGA AGTCTGCTCT CTGAGAGTA CCTGTAAACC TGTCCCATGG

93 D Y T L T I S S L Q P E D F A T Y Y C L Q H G E S P W T F G Q G T

801 AAGTGGAGA TCAACGAAC TGTGCTGCA CCACTCTGCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGC
TTCACCTCT AGTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTGCTCACT TTAGACCTTG ACAGAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGGAA GTTGATTAAC GCCCTCCAAT CGGTAACCTC CAGGAGAGT GTACACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGCTCT CTCGGTTTC ATGTCACCTT CCACCTATTG CCGGAGTTA GCCCATGAG GGTCTCTCA CAGTGTCTCG TCCTGTGCTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGCACC TACAGCCTCA GCAGCACCT GAGCTGAGC AAGCAGACT ACAGAAACA CAAAGTCTAC GCCTCGAAG TCACCCATCA GGGCTTGAGC
CCTGCTGG ATGTCGAGT GGTCTGGGA CTGCGACTCG TTTCTCTGA TGTCTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCGGACTCG

193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

1101 TCGCCCTGCA CAAAGAGCTT CAACAGGGA GAGTGTATAT TAAATCTCT ACGCCGAGC CATCTGGCG AGCTCGGTAC CCGGGATCT AGGCTTAACG
AGCGGCGAGT GTTCTCGAA GTTGTCCCT CTCAATTA ATTAGAGA TGCSCCTGC GTAGCACCGC TCGACCATG GGCOCCTAGA TCGGATTGC

226 S P V T K S F N R G E C O

Figure 20a

1201 CTCGGTTGCC GCGGGCGTT TTTTATGTT GCGACGCGC ATCTGAATG AACTGTGTGC GCAGGTAGAA GTTTTGGAGA TTATCGTCAC TGAATGCTT
GAGCCACGG CGGCCGCGAA AAATAACAA CCGCTGCGG TAGAGTTAC TTGACACAG CGTCCATCTT CCAAACTCT AATAGCAGTG ACGTTAGAA

1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTTATC AGTAGAGGG GGCCTGTAC GAGTAAAGC CCGATGCCAG CATTCCTGAC GAGATACGG
GCGTTATACC GCGTTTACT GGTGTGCC AACTAATAG TCCATCTCC CCGGACATG CTCATTTCC GGTACGGTC GTAAGGACTG CTGCTATGCC

1401 AGCTGTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACAG CCGAGACTTA
TCGACGCGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAT TTTCATATG AAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT

1501 TAGTGGCTTT GTTTTATTT TTTAATGAT TTGTAAGTAG TAGCAAGTT CAAGTAAAAA GGGTATCTAG AATTATGAG AAGATATCG CATTTCTTCT
ATCAGGAAA CAAAAATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAATTTT CCATAGATC TTAACTATTC TTCTATAGC GTAAAGAGA
M K K N I A F L L
^Still Signal Sequence TIR-1

1601 TGCACTATG TTCGTTTTT CTATTTGCTAC AAAGCGGTAC GCTGAGTTTC AGCTGTGGA GTCTGGGGT GGCCTGGTGC AGCCAGGGG CTCACCTCGT
ACGTAGATAC AAGCAAAAA GATAACGATG TTTGCGCATG CGACTCCAAG TCGACCACTT CAGACCGCA CCGGACCAAG TCGGTCCGCC GAGTGGGA
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R

^Anti-Tissue Factor Heavy Chain

1701 TTGTCCTGTG CAGCTTCTTG CTTCATATTT AAGAGTACT ACATGACTG GGTCCGTAC GCGCCGGGT AAGGCTTGA ATGGTTTGA TTGATGATC
AACAGGACAC GTCGAAGAC GAAATTATA TTCTTCATGA TGACGTGAC CCAGGAGTC CGGGGCCAT TCCCGGACT TACCAACCT AACTAATAG
43 L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E W V G L I D P

1801 CAGAGCAAGG CAACAGATC TATGACCGA AGTTCCAGG CCGTCCACT ATAGCGCTG ACATTTCCA AAACACAGCA TACCTGCAGA TGAACAGCT
GTCTGTTC GTTGTGCTAG ATACTGGCT TCAAGTCTT GGCACGTGA TATTCGCGC TGTTAAGTT TTTGTGCTG ATGACGCTT ACTTGTGGA
77 E Q G N T I Y D P K F Q D R A T I S A D N S K N T A Y L Q M N S L

1901 GCGTGTGAG GACACTGCG TCTATTATG TGCTCGAGAC AGCGCGCTT ACTTCGACTA CTGGGCTCA GGAACCTGG TCACCGTCT CTCGGCTCC
CGCAGACTC CTGTGACGGC AGATAATAC ACAGCTCTG TGCCGGGAA TGAAGCTGAT GACCCGCTG CTTGGGACC AGTGGCAGAG GAGCCGGAGG
110 R A E D T A V Y Y C A R D T A A Y F D Y W G Q G T L V T V S S A S

2001 ACCAAGGCG CATCGTCTT CCGCTGGCA CCTCTTCA AGACACCTC TGCGGCGACA GCGGCGCTG GCTGCTGTG CAAGGACTAC TTCCCGAAG
TGCTTCCGG GTAGCCAGAA GGGGACCGT TCTGTGAG ACCCCGCTG CCGCGGACC CGACGACCA GTTCTGTATG AAGGGCTTG
143 T K G P S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P

2101 GGTGACGGT GTCGTGGAAC TCAGGCGCC TGACAGGG CGTGACACC TTCCCGCTG TCCTACATC CTCAGGACTC TACTCCCTCA GACGCTGTG
GCCACTGCA CAGCACCTTG AGTCGCGGG ACTGTGCGC CCACGTGAG AAGGGCGAC AGGATGTCAG GAGTCTGAG ATGAGGAGT CGTCGACCA
177 V T V S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V

2201 GACTGTGCC TCTAGCAGT TGGGACCCA GACCTACAT TGCACGTGA ATCACAGCC CAGCACACC AAGTTGGACA AGAAGTTGA GCCCAATCT
CTGACACGG AGATGTCGA ACCGTGGT CTGGATGAG ACCTGCTGCT TGTGTGCG GTCTGTGAG TTCCACCTGT TCTTCACT CGGGTTTGA
210 T V P S S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S

2301 TGTGACAAA CTCACACATG CCCACCTGC CCGACCTTG AACTCTGGG GGGACGTCA GTCTTCTCT TCCGCCAAA ACCCAAGAC ACCCTCATGA
ACACTGTTT GAGTGTGAC GGTGGCAGG GGTGTGGAC TTGAGACCC CCTTGGAGT CTAGAGAG AGGGGGTTT TGGTTCTCTG TGGGAGTACT
243 C D K T H T C P P C P A P E L L G G P S V F L F P P K P K D T L M I

2401 TCTCCGGAC CCTGAGGTC ACATGCTGG TGTGAGACT GAGCCAGAA GACCTGAGG TCAAGTTCAA CTGGTACGT GACGGCGTGG AGTGCATAA
AGAGGCGCTG GGGACTCCAG TGTAGGCACC ACCACTGCA CTGGTGTCT TGGGACTCC AGTTCAAGTT GACCATGAC CTGCGCACCC TCCACGATT
277 S R T P E V T C V V V D V S H E D P E V K F N W Y V D G V E V H N

Figure 20b

2501 TGCCAAGACA AAGCCGCGGG AGGAGCAGTA CAACAGCAAG TACCGGTGG TCAGGTCCT CACCGTCCTG CACCAAGGACT GGCTGAATGG CAAGGAGTAC
ACGGTTCTGT TTGCGGCGCC TCCTCGTCAT GTTGTCGTGC ATGGCACACC AGTCGACAGA GTGGCAGGAC GTGGTCTTGA CCGACTTACC GTTCCCTCATG
310 A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W L N G K E Y

2601 AAGTGCAAGG TCTCCAACAA AGCCCTCCCA GCCCCATCG AGAAACACNT CTCACAGCC AAGGGGAGC CCGAGAAACC ACAGGTGTAC ACCCTGCCCC
TTACGTTCC AGAGGTGTG TTGCGAGGGT CCGGGGTAGC TCTTTGGTA GAGTTTCGG TTTCCTGTCG GGGCTCTTGG TGTCCACATG TGGGAGGGG
343 K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P

2701 CATCCCGGA AGAGTAGC AAGAACAGG TCAGCCTGAC CTGCTGTGTC AAGGCTTCT ATCCAGCGA CATCCCGTG GAGTGGAGA GCAATGGCA
GTAGGCCCT TCTCTACTGG TTCTTGTTCC AGTCGACTG GACGACCAG TTTCGAGA TAGGTCGCT GTAGCGGAC CTCACCTCT CGTTACCCGT
377 S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q

2801 GCCGAGAAC AACTACAAGA CCAGCCTCC CGTGTGGAC TCCGACGGCT CCTTCTTCT CTACAGCAAG CTCACCGTG ACRAGAGCAG GTGGCAGCAG
CGGCTCTTG TTGATGTTCT GGTGGGAGG GCAGACCTG AGGCTGCCGA GGAAGAAGA GATGTCGTTG GAGTGGCACC TGTTCTGTC CACCGTCGTC
410 P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q

2901 GGGACGTCT TCTATGTC CGTATGCT GAGGCTCTGC ACAACACTA CACGAGAAG AGCTCTTCC TGTCTCCGG TAAATAAGCA TGGGACGGCC
CCCTTGCGA AGAGTACGAG GCACTACGTA CTCGAGAGS TGTGGTGAT GTGCTCTTC TCGGAGAGG ACAGAGGCC ATTTATTCGT ACCTGCCGG
443 G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K O

3001 CTAGAGTCCC TAACGTCGG TTGCGCGCG GCGTTTTTA TTGTTAATC ATGTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG TTTATCACAG
GATCTCAGG ATTGCGAGC AACGCGCGC CGCAAAAT AACAATTAG TACAACGTG CGAATAGTAG CTATTTCGAA TTACGCCATC AAATAGTGC

3101 TTAAATTGCT AACGCAGTCA GGCACCGTGT ATGAATCTA ACAATPGCGT CATGTCATC CTCGGCACCG TCACCTGGA TGCTGTAGGC ATAGGCTTGG
AATTTAACA TTGCGTCAGT CCGTGGCACA TACTTTAGAT TGTTACGGA GTAGCAGTAG GAGCGGTGGC AGTGGGACCT ACGACATCCG TATCCGAACC

3201 TTATGCCGT ACTGCCGGG CTCTTGCGG ATATGTCGA TTCCGACAGC ATCGCCAGTC ACTATGGCT GCTGTAGCG CTATATGCGT TGATGCAATT
AATACGGCCA TGACGGCCG GAGAACGCC TATAGCAGT AAGCTGTGCG TAGCGTFCAG TGATACCGCA CGACGATCGC GATATACGCA ACTACGTTAA

3301

Figure 20c

1 GAATTCACCT TCTCCATACT TTGATAAGG AATACAGAC ATGAATAATC TCATTGCTGA GTTGTAATTT AAGTTGCCC AAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGTATGA AACCTATTCC TTATGTCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCGACGGG TTTTCTCTCT TCTCAGCTTA

101 GAACTGTGT CCGAGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCCAAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC CGGTCCATCT TCGAACCTC TAATAGCACT GACGTTAGA AGCGTTATAC CGCGTTTATC TGGTTGTGCG CAACCTAATA GTCCATCTCC

201 GGGCGCTGTA CGAGTAAAG CCGATGCGCA GCATTCCTGA CGAGCAACG GAGCTGCTGC GCGATTAGT AAGAAGCTTA TTGAAGCAAC CTGCTCAGTA
CCCGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTCCTATG CTCGACGAG CGCTAATGCA TTTCTUCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCTATA AGTGTCTCAG GCGAGACTT ATAGTCGCTT TGTTTTATTT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCATTTA GAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCAA AAAAAATAA AAAATTACAT AACATTGAT CATGGTTCA

401 TCACGTAAAA AGGTATCTA GAATTATGAA GAAGAAATAT GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAAGCGSTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAGAAG AAGCTAGATA CAAGCAAAA AGATAAGCAT GTTTGCGCAT CCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII Signal TIR ~1 Anti-VEGF Light chain

501 CAGTTGACCC AGTCCCGAG CTCCTGTCC GCTCTGTGG GCGATAGGGT CACCATCAC TCCAGCGCAA GTCAAGTAT TAGCAACTAT TTAACTGGT
GTCAACTGGG TCAGGGCTC GAGGGACAGG CGGACACACC CGCTATCCCA GTGTAGTGG AGTGGGCTT CAGTCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGNAAA GCTCGAAG TACTGATTTA CTTCACTCC TCTCTCCACT CTGAGTCCC TTCTGCTTC TCTGATCCG GTTCTGGGAC
TAGTTGTCTT TGTCTCTTTT CGAGCTTTC ATGACTAAAT GAAGTGGAG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCTCG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGAATTCAT CTGACCATCA GCAGTCTGCA GCCAAGAGAC TTGCGAACTT ATTACTGICA ACAGTATAGC ACGTGGCGGT GGAAGTTTGG ACAGGTATCC
CCTAAAGTGA GACTGGTAGT CGTCAGAGCT CGGCTCTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCAGGCA CCGTCAAACC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGGTGGAGA TCAAGGAAC TGTGGCTGCA CCACTCTCT TCACTCTCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGTC
TTCCACCTCT AGTTTGTCTG ACACCGAGCT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTGCTCACT TTAGACCTTG ACAGAGACAA CACACGAGC

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATTAATT CTATCCAGA GAGGCCAAG TACAGTGGAA GTTGATAAC GCCCTCCAA CTGCTCACTC CAGGAGACT GTCAAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTTA GCCCATGAG GTTCTCTCA CAGTGTCTCG TCCGTGCTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

1001 GGACAGCACC TACAGCTCA GCAGCACCT GACGCTGAGC AAGCAGACT ACAGAAACA CAAAGTCTAC GCTCGGAAG TCACCCATCA GGGCCTGAGC
CCTGCTGGG ATGTGGAGT CGTGGTGGG CTGCGACTCG TTTCTCTGTA TGCTTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCGGACTCG

193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGA GAGTGTAAAT TAATCTCTCT ACGCGGAGC CATCTGGG AGCTCGGTAC CCGGGATCT AGGCCTAACG
ACCGGAGCT GTTCTCGAA GTTGTCCCT CTCACAAITA AATTAGAGA TCGGCGCTGC GTACACCGC TCGAGCCATG GGGCCCTAGA TCCGGATTGC

226 S P V T K S F N R G E C O

Figure 21a

1201 CTCGGTGGC GCGGGCGTT TTTTATTGT GCGGACGGC ATCTCGAATG AACTGTGTG GACGATGAG GCTTTGGAGA TTATGTGTAC TGAATGTCTT
GAGCAACGG CGGCCCGCAA AATAAACAA CCGCTGCGG TAGAGTTTAC TTGACACAG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA

1301 CCAATATGG CGCAAATGA CCAACAGGG TTGATGATC AGTAGAGGG GCGCTGTAC GAGTAAAGC CGATGCCAG CATTCCTGAC GACGATACGG
GGTTATACC GCGTTTACT GGTGTGGCC AACTAACTAG TCCATCTCCC CCGGACATG CTCCATTTCC GGTACGGTC GTAAGGACTG CTGCTATGCC

1401 AGCTGCTGG CGAATAGTA AAGAAGTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTATATAA GTTGTACAG CCGAGACTTA
TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAIT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGTCTGAAT

1501 TAGTGGCTTT GTTTTATTT TTTAATGTAT TTGTAATCTAG TAGGCAAGTT CACGTAAAAA GGTATCTAG AATTATGAG AAGAATATCG CATTTCTTCT
ATCAGCGAAA CAAATAAATAA AATATACATA AACATGATC ATGCGTTCAA GTGCATTTT CCATAGATC TTAATACTTC TTCTTATAGC GTAAGAAGA

1601 TGCATCTATG TTGTTTCTTT CATTGCTAC AAACGGCTAC GCTGAGTTTC AGCTGGTGA GTCTGGCGGT GGCCTGGTGC AGCCAGGGG CTCACCTCGT
ACGTAGATAC AAGCAAAAA GATAACGATG TTGCGCATG CGACTCCAG TCGACCACT CAGACCGCA CCGGACCAAG TCGGTCCCC GAGTGAGCA

10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
^Anti-VEGF Heavy Chain

1701 TTGTCCTGT CAGCTTCTGG CTACGACTTC AGCAGCTAC GATGCTGAG TGCATGATG CATACTGAC CCAGGCACT TCCCGGACCT TACCAACCT ACCTAATTGT
AACAGGACAC GTCGAAGACC GATGCTGAG TGCATGATG CATACTGAC CCAGGCACT TCCCGGACCT TACCAACCT TACCAACCT ACCTAATTGT

43 L S C A A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T

1801 CCTATACGG TGAACCGACC TANGCTGGG AITTCAAAAG TCGTTTACT TTTTCTTTAG ACACCTCCAA AAGCAGCA TACTGTGAGA TGAACAGCCT
GGATATGCC ACTTGGCTG ATACAGGCC TAAAGTTTGC ASCAAAGTA AAGAANAATC TGTGGAGTT TCGTGTCTGT ATGAGCTCT ACTTGTCCGA

77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

1901 GCGGCTGAG GACATGCG TCTATTACTG TGCAAGTAC CCGTACTATT ACAGCAGAG CCACTGTGAT TCGACGCTT TCGACGCTT AACCCTGGTC
CGCGGACTC CTGTGAGGC AGATAATGAC ACGTTTCTAG GGCATGATAA TGCGTCTC GTGTGACATA AAGCTGCAGA CCCAGTTCC TTGGGACCAAG

110 R A E D T A V Y Y C A K Y P Y Y Y G T S H W Y F D V W G Q G T L V

2001 ACGTCTCCT CCGCTCCAC CAAGGGCCA TGGTCTTCC CCCTGGACC CTCTCCAAG AGCAGCTCTG GGGCACAGC GGCCTGGGC TGCCTGGTCA
TGGCAGGGA GCGGAGGTG GTTCCCGGT AGCCAGAGG GGGACGCTG GAGGAGTTT TCGTGGAGC CCCGTGTG CCGGACCCG ACGGACCCAGT

143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

2101 AGGACTACTT CCGGAACG GTGACGCTGT CGTGGAATC AGGCGCCCTG ACCAGCGGG TGCACACCTT CCGGCTGTC CTACAGTCTT CAGGACTCTA
TCTGTATGA GGGCTTGGC CACTGCCACA GCACCTTGA TCCGCGGAC TGTGCGCCG ACGTGTGAA GGGCCGACAG GATGTACGA GTCTGTAGAT

177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y

2201 CTCCTCAGC AGCTGTGA CTGTGCCCTC TAGCAGCTTG GGCACCCAGA CCTACATCTG CAACGTGAAT CACAGGCCA GCAACACCA GGTGGACAG
GAGGAGTCG TCGCACCACT GACAGGGAG ATCGTCGAAC CCGTGGTCT GGTGTGATG GATGTAGAC GTTGACATA GTGTCCGGT CCGTGTGTTT

210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K

2301 AAAGTTGAG CCAATCTTG TGACAAACT CACATGCT CACGTCGCC AGCAGCTGAA CTCCTGGGG GACGCTAGT CTTCTCTTTC CCCCCAAAC
TTTCAACTG GGTTAGAAC ACTGTTTGA GTGTGATG GTGTGATG GTGTGATG GTGTGATG GTGTGATG GTGTGATG GTGTGATG GTGTGATG GTGTGATG

243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P

2401 CCAAGGACAC CCTCATGATC TCCGGACCC CTGAGGTGAC ATGCTGTG GTGGAGTGA GCCAGAGA CCGTGGGTC AAGTTCACT GGTAGCTGA
GGTCTCTGT GAGTACTAG AGGCGCTGG GACTCCAGT TACGACAC CACTGCTCTT CCGTCTCTT CCGTCTCTT CCGTCTCTT CCGTCTCTT CCGTCTCTT

277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D

^STII Signal TIR-1

M K N I A F L L

Figure 21b

2501 CGGCGTGGAG GTGCATAATG CCAAGACAAA GCGCGGGAG GAGCAGTACA ACAGCACCTA CCGTGTGGTC AGGCTCTGCA CCAGGACTGG
GCGCACCTC CACGTATTAC GGTTCGTGTT CCGCGCCCTC CTCGTATGTT TGTGTGAT GGCACACAG TCGCAGGAGT GGCAGGAGT GGTCTGACC
310 G V E V H N A K T K P R E Q Y N S T Y R V V S V L T V L H Q D W

2601 CTGAATGCA AGGAGTACAA GTGCAAGGTC TCCAACAAG CCTCCACG CCCATCGAG AAAACCATCT CCAAGCCAA AGGCAGGCC CGAGAACCAC
GACTTACCGT TCCTCATGTT CAGCTTCCAG AGTTGTTT GGGAGGTG GGGTAGTCTC TTITGGTAGA GGTTCGGTT TCCGTCGGG GCTCTTGGT
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q

2701 AGGTGTACAC CCTGCCCCCA TCCCGGGAAG AGATGACCAA GAACAGGTC AGCCTGACCT GCCTGTGCAA AGCTTCTAT CCCAGCACA TCGCCGTGGA
TCCACATGTG GGACGGGGT AGGGCCCTTC TCTACTGTT TCTGTCCAG TCGGACTGGA CGGACCACTT TCCGAAGATA GGTGCTGTGT AGCGCACCT
377 V Y T L P P S R E M T K N Q V S L T C L V K G F Y P S D I A V E

2801 GTGGGAGAGC AATGGGAGC CGGAGAACA CTACAAGAC AGCCTCCCG TCTGTGACTC CGACGGCTCC TTCTTCTCT ACAGCAAGCT CACCGTGGAC
CACCTCTCG TTACCGTCG GCCTCTGTT GATGTTCTGG TCGGAGGCG ACAGCTGAG GCTCCCGAGG AAGAAGGAGA TGTGTTTGA GTGCACCTG
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D

2901 AAGAGCAGT GGCAGCAGG GAACTCTTC TCATGCTCG TGATGATGA GGCTCTGCAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGTA
TTCTGCTCA CCGTCGTCCC CTTCAGAG AGTACAGGC ACTACGACT CCGAGACGTG TTGGTGATG GCCTCTTCTC GGAGAGGAC AGAGGCCAT
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K

3001 AATAAGCATG CGACGGCCCT AGAGTCCCTA ACGCTCGTT GCGCGCGGGC GTTTTATT GTTAACTCAT GTTTGACAG TTATCATCGA TAAGCTTTAA
TTATTCTGAC GCTGCCGGGA TCTAGGGAT TCGAGCCAA CGCGCGCCCG CAAAAATPA CAATTGATA CAATGTCG AATAGTAGCT ATTGAAATT
477 O

3101 TCGGGTAGTT TATCAGATT AAATTGCTAA CGCAGTCAG CACCTGTAT GAAATCTAAC AATCGCTCA TCGTATCCT CGGCACCGTC ACCCTGGATG
ACGCCATCA ATAGTGTCAA TTACAGATT CGCTCAGTCC GTGGCACATA CTTTAGATTG TTACGCGAGT AGCAGTAGGA GCGGTGGCAG TGGGACCTAC
Start Tet Resistance Coding Sequence

3201 CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGGCTT CTTGCGGGAT ATCTCCATT CCGACAGAT CGCCAGTAC TATGGCTGC TGCTAGCGCT
GACATCCGTA TCCGAACCAA TACGGCCATG ACGGCCCGA GAACGCCCTA TAGCAGTAA GCTGTGCTA GCGGTGAGT ATACCGCAG ACGATCGCA

3301

Figure 21c

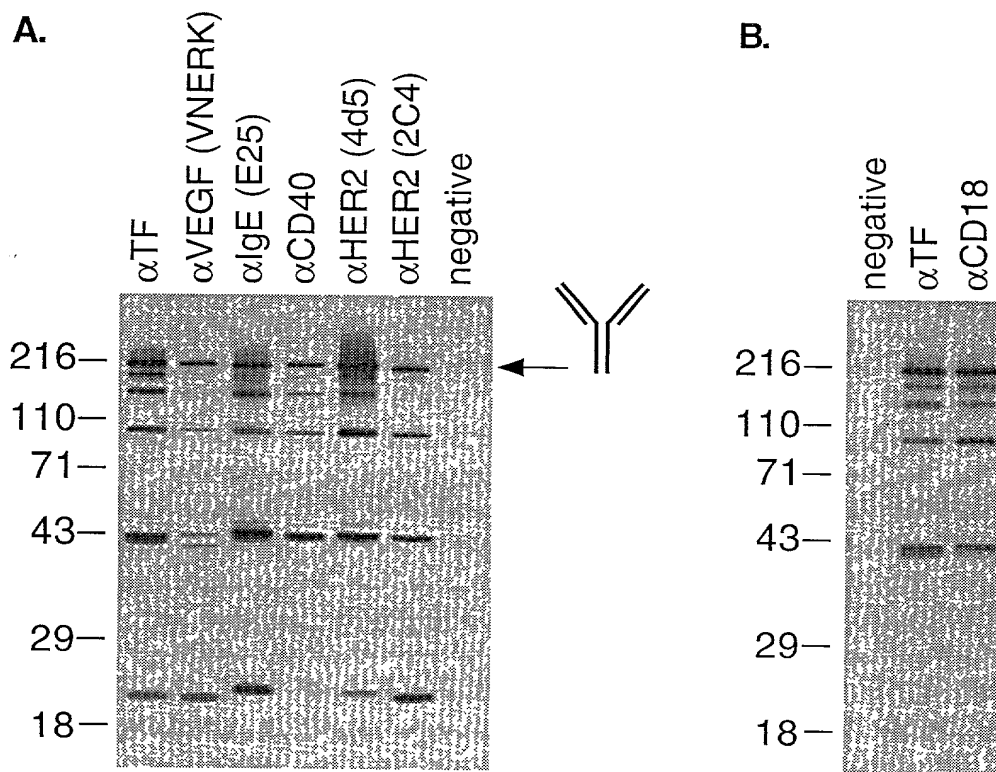


Figure 22